

### Listing of Claims

1-4. (Canceled)

5. (Currently amended) An isolated nucleic acid molecule encoding a RFX4\_v3 polypeptide, wherein the polypeptide comprises:

- a) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 8;
  - b) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 8, wherein fourteen consecutive amino acids within the N-terminal sequence of the polypeptide are identical to residues 1-14 of SEQ ID NO: 8; or
  - c) the amino acid sequence ~~set forth as~~ of SEQ ID NO: 8,
- wherein the polypeptide in a), b), or c) has RFX4\_v3 activity.

6. (Currently amended) The nucleic acid molecule of claim 5 comprising:  
a nucleic acid sequence at least 95% identical to the nucleic acid sequence of SEQ ID NO: 37.

7. (Currently amended) ~~The~~ An isolated nucleic acid molecule encoding a RFX4\_v3 polypeptide, comprising a ~~of claim 18, wherein the~~ nucleic acid sequence is at least 95% identical to the nucleic acid sequence of SEQ ID NO: 37, SEQ ID NO: 38 or SEQ ID NO: 39.

8. (Currently amended) The nucleic acid molecule of claim 6, wherein the nucleic acid sequence is at least 99% identical to the nucleic acid sequence of SEQ ID NO: 37.

9. (Previously presented) The nucleic acid molecule of claim 5 operably linked to a heterologous promoter.

10. (Previously presented) The nucleic acid molecule of claim 9, wherein the heterologous promoter comprises SEQ ID NO: 11 or SEQ ID NO: 12.

11. (Previously presented) A vector comprising the nucleic acid molecule of claim 5.

12. (Previously presented) An *in vitro* host cell transformed with the vector of claim 11.

13. (Previously presented) The *in vitro* host cell of claim 12, wherein the host cell is a plant cell, an animal cell, or a prokaryotic cell.

14. (Previously presented) A composition comprising the nucleic acid molecule of claim 5.

15. (Currently amended) An isolated nucleic acid molecule that hybridizes under conditions of high stringency to a polynucleotide consisting of nucleotides 1-42 of a nucleic acid sequence selected from the group consisting of SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39, wherein the isolated nucleic acid molecule comprises at least ~~15~~20 contiguous nucleotides of nucleotides 1-42 of SEQ ID NO:37, SEQ ID NO: 38, or SEQ ID NO: 39, and wherein the isolated nucleic acid molecule encodes a RFX4\_v3 polypeptide at least 99% identical to the amino acid sequence of SEQ ID NO: 8, SEQ ID NO: 6, or SEQ ID NO: 10, respectively.

16-17. (Canceled)

18. (Previously presented) An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a RFX4\_v3 polypeptide comprising SEQ ID NO: 6, SEQ ID NO: 8, or SEQ ID NO: 10.

19. (Previously presented) A vector comprising the nucleic acid molecule of claim 15.

20. (Previously presented) An *in vitro* host cell transformed with the vector of claim 19.

21. (Previously presented) The *in vitro* host cell of claim 20, wherein the host cell is a plant cell, an animal cell, or a prokaryotic cell.

22-24. (Canceled)

25. (Currently amended) A method for producing a variant RFX4\_v3 polypeptide, wherein the method comprises:

mutagenizing a wild-type nucleic acid sequence ~~as set forth in~~ having SEQ ID NO: 37, SEQ ID NO: 38, or SEQ ID NO: 39;

expressing the mutagenized nucleic acid sequence; and

screening the variant ~~for a RFX4\_v3 polypeptide~~ for a RFX4\_v3 activity ~~to identify the variant of the RFX4\_v3 polypeptide~~, wherein the variant RFX4\_v3 polypeptide comprises:

a) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 8;

b) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 8, wherein fourteen consecutive amino acids within the N-terminal sequence of the polypeptide are identical to residues 1-14 of SEQ ID NO: 8; or

c) the amino acid sequence ~~set forth as~~ of SEQ ID NO: 8, wherein the polypeptide in a), b), or c) has RFX4\_v3 activity.

26. (Currently amended) A composition comprising a nucleic acid molecule that inhibits the binding of the polynucleotide of claim 15 to its complementary sequence, wherein the nucleic acid molecule comprises at least 20 contiguous nucleotides of nucleotides 1-42 of SEQ ID NO: 37, SEQ ID NO: 38, or SEQ ID NO: 39 and encodes a RFX4\_v3 polypeptide at least 99% identical to the amino acid sequence of SEQ ID NO: 8, SEQ ID NO: 6, or SEQ ID NO: 10, respectively.

27. (Previously presented) The isolated nucleic acid molecule of claim 15, wherein the isolated nucleic acid molecule hybridizes under conditions of high stringency to the polynucleotide consisting of nucleotides 1-42 of SEQ ID NO: 37.

28. (Withdrawn) A method for detecting a nucleic acid molecule in a biological sample, comprising:

hybridizing a polynucleotide to the nucleic acid molecule of claim 5 to produce a hybridization complex, wherein the polynucleotide hybridizes under conditions of high stringency to nucleotides 1-42 of SEQ ID NO: 37, SEQ ID NO: 38, or SEQ ID NO: 39;

detecting the hybridization complex, wherein the presence of the hybridization complex indicates the presence of the nucleic acid molecule encoding RFX4\_v3 in the biological sample, thereby detecting the nucleic acid molecule in the biological sample.

29. (Withdrawn) The method of claim 28, wherein the polynucleotide hybridizes to SEQ ID NO: 37.

30. (Withdrawn) The method of claim 28, further comprising amplifying the nucleic acid molecule prior to hybridizing with the polynucleotide.

31. (Withdrawn) A method of identifying a subject at risk of developing RFX4\_v3 linked hydrocephalus, comprising detecting in the subject a mutation in the nucleic acid molecule of claim 5, wherein the mutation in the nucleic acid molecule alters the RFX4\_v3 polypeptide, thereby identifying a subject at risk of developing RFX4\_v3 linked hydrocephalus.

32. (Canceled)

33. (Withdrawn) The method of claim 31, wherein detecting the mutation in the RFX4\_v3 nucleic acid molecule comprises performing a hybridization analysis with a nucleic acid probe that detects the mutation in the RFX4\_v3 nucleic acid molecule.

34. (Withdrawn) The method of claim 31, wherein detecting the mutation comprises identifying an individual carrying a mutated RFX4\_v3 allele, wherein the method comprises: providing a nucleic acid from the subject, wherein the nucleic acid comprises a RFX4\_v3 allele; and

detecting a mutation in the nucleic acid that results in phenotypic expression of congenital hydrocephalus.

35. (Withdrawn) The method of claim 34, wherein the mutation is in the RFX4\_v3 allele.
36. (Withdrawn) The method of claim 31, wherein the method comprises detecting the mutation in the RFX4\_v3 polypeptide.
37. (Withdrawn) The method of claim 36, wherein the method comprises detecting an abnormality in expression of the RFX4\_v3 polypeptide.
38. (Withdrawn) The method of claim 37, wherein the method detects a reduced expression of the RFX4\_v3 polypeptide.
39. (Withdrawn) The method of claim 36, wherein the method comprises providing a polypeptide from the subject, and detecting a mutation in the sequence encoding the polypeptide, wherein the polypeptide comprises the RFX4\_v3 polypeptide and wherein the mutation results in phenotypic expression of congenital hydrocephalus.
40. (Withdrawn) The method of claim 31, comprising obtaining a biological sample from the subject, and detecting in the biological sample the mutation in the RFX4\_v3 polypeptide or in the RFX4\_v3 nucleotide sequence.
41. (Withdrawn) The method of claim 40, wherein the biological sample comprises blood, amniotic fluid, plasma, or cerebral spinal fluid.
42. (Canceled)
43. (Withdrawn) The method of claim 38, wherein detecting the reduced expression of the RFX4\_v3 polypeptide comprises using RFX4\_v1 specific antibodies.
44. (Withdrawn and currently amended) A kit for determining if a subject is a carrier of a mutated RFX4\_v3 gene, wherein the kit comprises:

a reagent that specifically detects a mutation in ~~a~~the isolated nucleic acid molecule of claim 5RFX4\_v3 allele, and

instructions for determining whether the subject is at increased risk of expressing congenital hydrocephalus if the reagent specifically detects the mutation.

45. (Withdrawn) The kit of claim 44, wherein the reagent comprises a nucleic acid probe that specifically hybridizes under conditions of high stringency to a nucleic acid sequence of SEQ ID NO: 37, SEQ ID NO: 38 or SEQ ID NO: 39.

46. (Withdrawn) The kit of claim 44, wherein the reagent comprises an antibody that specifically binds the protein expressed by the isolated nucleic acid molecule.

47-48. (Canceled)

49. (Withdrawn) An antibody that specifically binds the polypeptide encoded by the isolated nucleic acid of claim 5.

50-58. (Canceled)

59. (Withdrawn) A pharmaceutical composition, comprising:

a) a therapeutically effective amount of the polypeptide encoded by the isolated nucleic acid molecule of claim 5, the isolated nucleic acid molecule of claim 5, or a therapeutically effective variant or portion thereof; and

b) a pharmaceutically acceptable carrier.

60-64. (Canceled)

65. (Currently amended) The isolated nucleic acid molecule of claim 5, wherein the polypeptide comprises an amino acid sequence at least 99% identical to ~~an~~the amino acid sequence ~~set forth as of~~SEQ ID NO: 8.

66-67. (Canceled)

68. (Previously presented) The isolated nucleic acid molecule of claim 5, wherein the RFX4\_v3 polypeptide inhibits the phenotypic expression of congenital hydrocephalus.

69. (Previously presented) The isolated nucleic acid molecule of claim 5, wherein the polypeptide encoded by the nucleic acid molecule is bound by a RFX4\_v3 specific antibody.

70-73. (Canceled)

74. (Previously presented) An isolated nucleic acid molecule encoding a RFX4\_v3 polypeptide having RFX4\_v3 activity, wherein the polypeptide comprises SEQ ID NO: 8.

75. (Previously presented) An isolated nucleic acid molecule encoding a RFX4\_v3 polypeptide having RFX4\_v3 activity, wherein the isolated nucleic acid molecule comprises SEQ ID NO: 37.

76. (Currently amended) The isolated nucleic acid molecule of claim 5, wherein the isolated nucleic acid molecule encodes a RFX4\_v3 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 8, wherein fourteen consecutive amino acids within the N-terminal sequence of the polypeptide are identical to residues 1-14 of SEQ ID NO: 8.

77. (Canceled)

78. (New) The nucleic acid molecule of claim 7, wherein the nucleic acid sequence is at least 99% identical to the nucleic acid sequence of SEQ ID NO: 38.

79. (New) The nucleic acid molecule of claim 78, wherein the nucleic acid sequence comprises SEQ ID NO: 38.

80. (New) The nucleic acid molecule of claim 7, wherein the nucleic acid sequence is at least 99% identical to the nucleic acid sequence of SEQ ID NO: 39.

81. (New) The nucleic acid molecule of claim 80, wherein the nucleic acid sequence comprises SEQ ID NO: 39.

82. (New) An isolated nucleic acid molecule encoding a RFX4\_v3 polypeptide, consisting of the nucleic acid sequence of SEQ ID NO: 37, SEQ ID NO: 38, or SEQ ID NO: 39.